Journal of Forensic and Legal Medicine 19 (2012) 291–293

Contents lists available at SciVerse ScienceDirect

Journal of Forensic and Legal Medicine

journal homepage: www.elsevier.com/locate/jflm

Original communication

Electrocardiographic findings and cardiac manifestations in acute aluminum phosphide poisoning

Kambiz Soltaninejad PharmD., Ph.D, Assistant Professor [a], Mohammad-Reza Beyranvand M.D., Associate Professor [b], Seyed-Akbar Momenzadeh M.D. [b], Shahin Shadnia M.D., Ph.D, Associate Professor [c,*]

[a] Department of Forensic Toxicology, Legal Medicine Research Center, Legal Medicine Organization of Iran, Tehran, Iran
[b] Internal Medicine Department, Loghman Hakim Hospital, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[c] Clinical Toxicology Department, Loghman Hakim Hospital Poison Center, Faculty of Medicine, and Toxicological Research Center (TRC), Shahid Beheshti University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article history:
Received 27 January 2011
Received in revised form
31 December 2011
Accepted 13 February 2012
Available online 8 April 2012

Keywords:
Aluminium phosphide
Cardiac
Electrocardiogram
Mortality
Poisoning

ABSTRACT

Aluminium phosphide (AlP) poisoning has a high mortality due to cardiovascular involvement. In this study, we evaluated the frequency of cardiac manifestations and electrocardiographic (ECG) findings in 20 patients with acute AlP poisoning, who were admitted to the intensive care unit (ICU) in Tehran, Iran, over a period of 6 months (between October 2008 and April 2009). The sex, age, cause and manner of ingestion, number of ingested AlP tablets, cardiac and ECG manifestations, creatine phosphokinase (CPK), CPK-myocardial band (CPK-mb) and troponin-T (TnT) were extracted from the patients' files. All data were analysed with Statistical Package for the Social Sciences (SPSS) software.

The majority (60%) of patients were male. The mean age was 27 ± 8.7 years. The mortality rate was 40%. In all of the patients, the cause of poisoning was intentional suicide and ingestion was the route of exposure. The mean number of ingested AlP tablets per patient was 2.2 ± 1.1. The average time interval between admission and cardiovascular manifestations or ECG findings was 168.8 ± 116.2 min. The range of systolic (SBP) and diastolic blood pressure was 60–130 mmHg and 40–70 mmHg, respectively. Dysrhythmia was observed in nine (45%) cases. Elevation of the ST segment was seen in nine cases (45%). Seven patients (35%) had prolonged QTc intervals. Bundle branch block (BBB) was observed in four (20%) patients. In nine (45%) patients, the serum cardiac TnT qualitative assay was positive. There were no significant differences between normal and abnormal ECG groups according to sex, age, number and manner of ingested AlP tablets and SBP. There was a significant correlation between cardiac manifestations and ECG findings and TnT-positive results with mortality in acute AlP poisoning.

1. Introduction

Aluminium phosphide (AlP) is a pesticide used to protect stored grains.[1] It is known as 'rice tablet' and sold under the brand name 'Phostoxin®' in Iran.[2] The incidence and mortality rate due to acute AlP poisoning is comparatively high in Iran.[3] AlP forms toxic phosphine (PH_3) gas following contact with water, moisture or the acidic content in the stomach.[1,4]

The heart and lungs are the target organs in acute AlP poisoning, although multi-organ system failure may occur. Most deaths occur within the first 12–24 h, usually because of cardiovascular toxicity.[1]

There are inconsistent studies about cardiac manifestations and electrocardiographic (ECG) findings in acute AlP poisoning and the outcome of patients.[5–7] In the present study, we investigated cardiac manifestations and ECG changes in 20 acute AlP self-inflicted poison cases.

2. Material and methods

Over a 6-month period (between October 2008 and April 2009), 20 patients with acute AlP poisoning, who were admitted to the intensive care unit (ICU) of Loghman Hakim Hospital Poison Center (LHHPC) in Tehran, Iran, were evaluated. Acute AlP-intoxicated patients with no history of cardiovascular disease and no co-ingestion of any other drugs were included in the study. The toxicological screening analysis for tricyclic antidepressants, benzodiazepines, acetaminophen, salicylates, tramadol, opioids, methamphetamine and methylenedeoxy methamphetamine was performed on urine samples in all of the cases by immunochromatography and thin-layer chromatography methods.

* Corresponding author. Clinical Toxicology Department, Loghman Hakim Hospital Poison Center, Kamali Street, South Karegar Avenue, Tehran-1333431151, Iran. Tel.:/fax: 98 21 55424041.
E-mail address: shadniatrc@sbmu.ac.ir (S. Shadnia).

1752-928X/$ – see front matter © 2012 Elsevier Ltd and Faculty of Forensic and Legal Medicine. All rights reserved.
doi:10.1016/j.jflm.2012.02.005

Diagnosis of AlP poisoning was based on a definite history of AlP ingestion and clinical manifestations. In fatal cases, autopsy and toxicological and pathological investigations were performed in Tehran Legal Medicine Center (TLMC). Chemical analysis by the silver nitrate test for phosphine detection on stomach contents, liver and kidney samples along with the liver histopathological evaluation confirmed AlP intoxication.

The sex, age, cause and manner of ingestion, number of ingested AlP tablets and cardiac manifestations at the time of presentation were recorded. During the first 6 h after admission to the ICU, ECGs, including the rate, rhythm, ST/T abnormalities, conduction defects and measurement of PR and QT intervals were carried out on all patients. The QT interval was corrected (QTc) according to the formula of Bazett.[8] Analyses of creatine phosphokinase (CPK), CPK-myocardial band (CPK-mb) and troponin-T (TnT) were routinely done on admission to the ICU.

All data were analysed with Statistical Package for the Social Sciences (SPSS) software. The data were expressed as mean ± SD for continuous or discrete variables and as frequency and percentage for categorical variables. Fisher's Exact test was used for statistical comparison of qualitative variables. The normal distribution of quantitative variables was evaluated by the Kolmogorov–Smirnov test. The statistical comparison was done with the Mann–Whitney *U*-test for non-parametric variables and the independent Student *t*-test was used for parametric variables.

P-values of 0.05 or less were considered to be statistically significant.

The study protocol was approved by the ethical committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

3. Results

The majority (60%) of the patients were male. The mean age was 27 ± 8.7 years (range: 15–42 years). There was no significant difference between survivors and non-survivors according to sex or age (Table 1). The overall mortality rate was 40%. In all of the patients, the cause of poisoning was intentional suicide and ingestion was the route of exposure. The range of ingested AlP tablets was 0.5–4 tablets and there was no significant difference in the number of ingested tablets between survivors and non-survivors (2 ± 1.1 *vs.* 2.4 ± 1.1 tablets, respectively, Table 1).

The average time interval between hospital admission and cardiovascular manifestations or ECG findings was 168.8 ± 116.2 min (range: 60–570 min, Table 1). There was no significant difference in this time between survivors and non-survivors (Table 1).

The mean ± SD of systolic (SBP) and diastolic blood pressure was 94.7 ± 15.5 mmHg (60–130 mmHg) and 61.2 ± 10.4 mmHg (40–70 mmHg), respectively. The mean ± SD SBP in survivors (100.4 ± 14.5 mmHg) and non-survivors (86.1 ± 13.5 mmHg) was significantly different (Table 1). There was a significant reverse correlation between SBP and mortality ($r = -0.46$, $p = 0.04$).

Sinus rhythm and dysrhythmia were observed in 11 (55%) and nine (45%) cases, respectively. Seven patients showed atrial fibrillation and two cases had junctional rhythm. There was a significant difference between survivors and non-survivors regarding cardiac rhythm (Table 1). Further, there was a significant correlation between cardiac dysrhythmia and mortality ($r = 0.70$, $p = 0.001$). Elevation of the ST segment (>2 mm above the isoelectric line) was observed in nine cases (45%, six of the nine patients died). Patients with ST segment elevation had a statistically higher mortality rate than patients without ST segment elevation (66.7% *vs.* 18.2%, respectively). There was a significant correlation between ST segment elevation and mortality ($r = 0.49$, $p = 0.03$). Seven patients (35%) had a prolonged QTc interval. Bundle branch block (BBB) was observed in four (20%) patients. Three (15%) cases had left BBB and in one (5%) case, it was a right BBB.

Regarding the ECG findings, there were no significant differences between normal and abnormal ECG groups due to sex, age, number or manner of ingested AlP tablets, and SBP (Table 1).

In nine (45%) patients, the serum cardiac TnT qualitative assay was positive. In 16 (80%) patients, the CPK levels and the CPK to CPK-mb ratios were increased. The number of positive results of the serum cardiac TnT qualitative assay was significantly different

Table 1
Distribution of patients based on sex, age, number of ingested AlP tablets, manner of ingestion, time interval between hospital admission and cardiovascular manifestations or ECG findings, systolic blood pressure and ECG findings.

Parameter		All patients ($n = 20$)	Survivors ($n = 12$)	Non-Survivors ($n = 8$)	P[a]	Normal ECG ($n = 10$)	Abnormal ECG ($n = 10$)	P
		Mean ± SD (range)	Mean ± SD (range)	Mean ± SD (range)		Mean ± SD (range)	Mean ± SD (range)	
Sex	Male	12	8	4	0.39	7	5	0.33
	Female	8	4	4		3	5	
Age (Year)		27.2 ± 8.7 (15–42)	26.5 ± 7.8 (18–42)	28.1 ± 10.4 (15–39)	0.70	26.1 ± 8.9 (16–42)	28.2 ± 8.9 (15–39)	0.61
Number of Ingested AlP Tablet		2.2 ± 1.1 (0.5–4)	2 ± 1.1 (1–4)	2.4 ± 1.1 (0.5–4)	0.41	2 ± 1.2 (1–4)	2.3 ± 1.1 (0.5–4)	0.49
Manner of Ingestion	With water	9	6	3	0.58	5	4	0.16
	Without water	8	5	3		5	3	
	Unknown	3	1	2		0	3	
Time interval between hospital admission and cardio-vascular manifestations or ECG findings (minute)		168.8 ± 116.2 (60–570)	177.1 ± 141 (60–570)	156.3 ± 71.5 (60–300)	0.71			
Systolic blood pressure (mmHg)		94.7 ± 15.5 (60–130)	100.4 ± 14.5 (80–130)	86.1 ± 13.5 (60–105)	0.04*	95 ± 15.8 (75–130)	94.4 ± 16.1 (60–120)	0.93
Cardiac rhythm	Sinus rhythm	11	10	1	0.003*			
	Atrial Fibrillation	7	1	6				
	Junctional Rhythm	2	1	1				
ST. Segment changes	No change	11	9	2	0.04*			
	Elevation	9	3	6				

Data are mean ± SD. The difference between survivors and non-survivors and also groups with normal and abnormal ECG is significant at $^*P < 0.05$.
[a] '*P*' mentions survivors versus non-survivors.

between survivors and non-survivors ($p = 0.04$); but there was no significant difference between these groups based on the CPK levels or the CPK to CPK-mb ratios ($p = 0.10$ and $p = 0.54$, respectively). There was a significant correlation between TnT-positive results and mortality ($r = 0.49$, $p = 0.03$).

The main post-mortem histopathological findings in gross examination were congestion in liver, brain, kidney and lung. In microscopic examination, the liver showed central venous congestion, microvacuolisation, degeneration of hepatocytes and mononuclear infiltration. The main histopathological findings in other organs were lungs congestion, oedema, haemorrhage, collapse of alveoli and alveolar thickening. In the brain, cerebral oedema, degenerated Nissel granule in the cytoplasm and deeply stained degenerated eccentric nucleus in brain cortex were observed. Degenerated neurons and infiltration of round cells into the molecular layer in cerebellar tissue and cerebral oedema were the most frequent findings in the microscopic features of brain tissue. Changes in the kidneys included glomeruli and intra-pearanchymal congestion.

4. Discussion

This study showed that there were significant differences between survivors and non-survivors regarding SBP and ECG abnormalities. However, there was no significant difference between survivors and non-survivors regarding sex, age, number of ingested tablets, or the time interval between admission to the hospital and the onset of cardiovascular manifestations and/or ECG findings. These findings are similar to our previous studies.[3,9] The manner of ingestion in the two groups was not different in the present study, whereas our previous study had shown a significant difference in this regard.[9] This outcome may be related to the difference in sample size and the observed immediate vomiting after ingestion in most of the patients in the previous study.

Although Chugh et al. (1991) reported in their study that there was no effect of ECG abnormalities on mortality in AlP intoxicated cases,[5] in this study we showed there was a significant correlation between ECG abnormalities and mortality. This finding is in concordance with previous studies.[4,10] The results of the present study, such as cardiac dysrhythmia, ST segment elevation and increase in TnT levels, can be explained based on the action of PH_3. The effect of PH_3 on the heart is multifactorial. Phosphine inhibits cytochrome *c* oxidase.[10] The inhibition of mitochondrial respiration results in myocardial energy depletion, similar to that which occurs with ischaemia.[7] Phosphine poisoning also results in the generation of reactive oxygen species causing lipid peroxidation.[7,10] These effects can cause alterations in cardiac transmembrane action potentials leading to dysrhythmia, an ischaemia-like effect on metabolism and on the ECG, inducing focal areas of necrosis and cardiac failure.[11]

There are inconsistent reports that suggest normal and abnormal CPK-mb levels in spite of ECG changes in acute AlP poisoning.[12,13] According to the results of this study, it seems that CPK levels and the CPK to CPK-mb ratios are not reliable markers of cardiac injury in these cases. Specific cardiac enzymes such as TnT should be considered as possible markers of cardiac injury.

As the present study is a retrospective one, and the post-mortem heart histopathological evaluation in TLMC is uncommon in routine medicolegal investigations, we could not obtain any information about post-mortem heart histopathological findings in acute AlP poisoning. From this view, this is a limitation in our study. An additional limitation of this study is the low number of cases; hence, further prospective investigation with a larger number of patients also is suggested. Finally, because of the correlation between cardiac dysrhythmia and mortality observed in this study, a clinical trial on the effectiveness of prophylactic administration of anti-arrhythmic agents in acute AlP intoxication should be considered.

5. Conclusion

SBP, cardiac dysrhythmia, ST segment elevation and TnT-positive results could be considered as findings for prediction of mortality in acute AlP poisoning.

Conflict of interest
None declared.

Funding
None.

Ethical approval
The study protocol was approved by the ethical committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Acknowledgement

The authors wish to thank Professor A. Wallace Hayes for his sophisticated help in editing our paper.

References

1. Perry HE. Rodenticides. In: Shannon MW, Borron SW, Burns MJ, editors. *Haddad and Winchester's clinical management of poisoning and drug overdose*. Philadelphia: W.B. Saunders Co.; 2007. p. 1218. 1225–6.
2. Mehrpour O, Singh S. Rice tablet poisoning: a major concern in Iranian population. *Hum Exp Toxicol* 2010;**29**:701–2.
3. Shadnia S, Sasanian G, Allami P, Hosseini A, Ranjbar A, Amini-Shirazi N, et al. A retrospective 7-years study of aluminum phosphide poisoning in Tehran: opportunities for prevention. *Hum Exp Toxicol* 2009;**28**:209–13.
4. Gupta S, Ahlawat SK. Aluminum phosphide poisoning review. *J Toxicol Clin Toxicol* 1995;**33**:19–24.
5. Chugh SN, Chugh K, Ram S, Malhotra KC. Electrocardiographic abnormalities in aluminum phosphide poisoning with special reference to its incidence, pathogenesis, mortality and histopathology. *J Indian Med Assoc* 1991;**89**:32–5.
6. Gupta SK, Mabajan A, Verma V, Gupta A. A clinical study of aluminium phosphide poisoning. *JK Sci* 2002;**4**:79–82.
7. Proudfoot AT. Aluminium and zinc phosphide poisoning. *Clin Toxicol* 2009;**47**:89–100.
8. Bazett HC. An analysis of the time-relationship of electrocardiogram. *Heart* 1920;**7**:353–70.
9. Shadnia S, Mehrpour O, Soltaninejad K. A simplified acute physiology score in the prediction of acute aluminum phosphide poisoning outcome. *Indian J Med Sci* 2010;**64**:532–9.
10. Singh S, Bhalla A, Verma SK, Kaur A, Gill K. Cytochrome-c oxidase inhibition in AlP poisoned patients. *Clin Toxicol* 2006;**44**:155–8.
11. Akkaoui M, Achour S, Abidi K, Himdi B, Madani A, Zeggwagh AA, et al. Reversible myocardial injury associated with aluminum phosphide poisoning. *Clin Toxicol* 2007;**45**:728–31.
12. Soltaninejad K, Shadnia S, Ziyapour B, Brent J. Aluminum phosphide intoxication mimicking ischemic heart disease led to unjustified treatment with streptokinase. *Clin Toxicol* 2009;**47**:908–9.
13. Kaushik RM, Kaushik R, Mahajan SK. Subendocardial infarction in a young survivor of aluminium phosphide poisoning. *Hum Exp Toxicol* 2007;**26**:457–60.